# Clinical Policy: Palbociclib (Ibrance)

Reference Number: ERX.SPA.156
Effective Date: 01.11.17
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Palbociclib (Ibrance®) is an inhibitor of cyclin-dependent kinases 4 and 6 (CDK 4/6).

**FDA Approved Indication(s)**
Ibrance is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

- An aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men; or
- Fulvestrant in patients with disease progression following endocrine therapy.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Ibrance is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Breast Cancer** (must meet all)**:**

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has all of the following characteristics (a, b, and c):
   a. HR-positive (i.e., estrogen receptor (ER) and/or progesterone receptor (PR) positive);
   b. HER2-negative;
   c. Advanced, recurrent, or metastatic;
5. Ibrance is prescribed in combination with one of the following (a or b):
   a. An aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) as part of initial endocrine based therapy, and:
      i. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
   b. Fulvestrant;
6. If member is a premenopausal female, member has been treated with ovarian ablation or is receiving ovarian suppression (*see Appendix D*);
7. Member has not previously experienced disease progression on a CDK 4/6 inhibitor therapy (e.g., Verzenio®, Kisqali®);
8. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
9. Request meets one of the following (a or b):*
   a. Dose does not exceed 125 mg (1 capsule or tablet) per day on Days 1 to 21 of a 28-day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Commercial –** Length of Benefit
**Medicaid –** 6 months

**B. Soft Tissue Sarcoma (off-label)** (must meet all)**:**
1. Diagnosis of retroperitoneal well-differentiated/dedifferentiated liposarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable;
5. Prescribed as a single agent;
6. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Commercial –** Length of Benefit
**Medicaid –** 6 months

**C. Other diagnoses/indications**
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

**A. All Indications in Section I** (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Ibrance for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
4. If breast cancer, dose is ≥ 75 mg per day;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 125 mg (1 capsule or tablet) per day on Days 1 to 21 of a 28-day cycle;
   b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Commercial –** Length of Benefit
**Medicaid –** 12 months

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

**B.** Use as adjuvant therapy in early-stage (stage 0-III) breast cancer.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

CDK: cyclin-dependent kinase
ER: estrogen receptor
ET: endocrine therapy
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
iDFS: invasive disease-free survival
NCCN: National Comprehensive Cancer Network
PR: progesterone receptor

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

None reported

*Appendix D: General Information*

- For disease progression while on a CDK 4/6 inhibitor, there is no data to support retreatment with another CDK 4/6 inhibitor-containing regimen.
- Although the FDA labeled indication limits combination use with fulvestrant to second line for breast cancer, the NCCN recommends this combination as both first and second line (category 1).
- Beginning in April 2020, Pfizer announced they would be switching Ibrance from capsules to tablets. The tablets allow increased flexibility with administration, dose tracking (weekly blister packs), and address dietary concerns (do not contain lactose or gelatin). These formulations are bioequivalent.
- In the Phase 3 PALbociclib CoLlaborative Adjuvant Study (PALLAS) open-label trial, 5,760 patients with stage II-III HR+/HER2-negative early breast cancer were randomized to receive either 2 years of Ibrance with adjuvant endocrine therapy (ET), or ET alone. The primary objective was to compare invasive disease-free survival (iDFS) between arms. At the second interim data analysis, after a median follow-up of 23.7 months (351 events), iDFS was similar between the two arms, with 3-year iDFS of 88.2% for Ibrance plus ET, and 88.5% for ET alone (HR 0.93, 95% CI 0.76-1.15), crossing a pre-specified futility boundary.
- Ovarian ablation may be accomplished by surgical oophorectomy or by ovarian irradiation. Ovarian suppression utilizes luteinizing hormone-releasing hormone (LHRH) agonists that result in suppression of luteinizing hormone and release of follicle-stimulating hormone from pituitary and reduction in ovarian estrogen production. LHRH agonists include goserelin and leuprolide.

## V. Dosage and Administration

| Indication | Dosing Regimen* | Maximum Dose |
|---|---|---|
| Breast cancer | 125 mg PO QD for 21 consecutive days followed by 7 days off treatment | 125 mg/day |

**If a dose reduction to < 75 mg/day is required, therapy should be discontinued.*

## VI. Product Availability

- Capsules: 75 mg, 100 mg, 125 mg
- Tablets: 75 mg, 100 mg, 125 mg

## VII. References

1. Ibrance Capsules Prescribing Information. New York, NY; Pfizer Labs; September 2019. Available at: www.ibrance.com/. Accessed June 24, 2021.
2. Ibrance Tablets Prescribing Information. New York, NY; Pfizer Labs; November 2019. Available at: www.ibrance.com/. Accessed June 24, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 23, 2021.

4. National Comprehensive Cancer Network. Breast Cancer Version 4.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed June 24, 2021.
5. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed July 14, 2020.
6. Dickson MA, Tap WD, Keohan ML, et al. Phase II trial of the CDK4 inhibitor PD0332991 in patients with advanced CDK4-amplified well differentiated or dedifferentiated liposarcoma. J Clin Oncol 2013;31(16):2024-2028.
7. Mayer EL, Gnant MI, DeMichele A, et al. PALLAS: A randomized phase III trial of adjuvant palbociclib with endocrine therapy versus endocrine therapy alone for HR+/HER2- early breast cancer. Presented at: European Society of Medical Oncology (ESMO) Virtual Congress 2020; September 19-21, 2020. LBA12.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 1Q18 annual review:<br>Converted to new template; added prescriber specialty requirement; added max dosing criteria; modified approval durations to length of benefit. | 11.17 | 02.18 |
| 4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added age; added specialist involvement in care for soft tissue sarcomas; references reviewed and updated. | 07.05.18 | 11.18 |
| No significant changes: added updated FDA indication for use in men; no change to criteria required. | 04.10.19 | |
| 4Q 2019 annual review: no significant changes; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated. | 08.09.19 | 11.19 |
| Added that member has not previously failed another CDK 4/6 inhibitor therapy for breast cancer. | 02.18.20 | 05.20 |
| Added tablet formulation. | 08.18.20 | |
| 4Q 2020 annual review: for breast cancer, modified to allow first-line use with fulvestrant per NCCN category 1 recommendation; for retroperitoneal liposarcoma, modified to allow only unresectable disease (removed metastatic and progressive options) per NCCN category 2A recommendation; added coverage exclusion for use as adjuvant therapy for early stage (stage II-III) breast cancer, based on PALLAS trial results; references reviewed and updated. | 10.01.20 | 11.20 |
| Breast cancer: clarified that combination use with an aromatase inhibitor should be for initial endocrine based therapy per FDA/NCCN and added that premenopausal women should be treated with ovarian ablation/suppression per NCCN; all indications: added requirement for no concurrent use with another CDK 4/6 inhibitor therapy. | 06.24.21 | 08.21 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.